



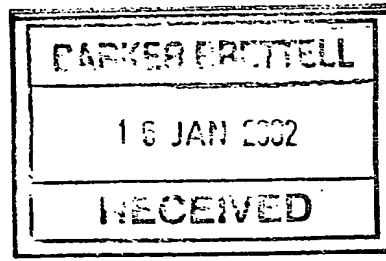
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Datum/Date
14 01. 2002

Zeichen/Ref./Réf. JL2042	Anmeldung Nr./Application No./Demande n°//Patent Nr./Patent No./Brevet n° 97937999.7-2107/US9712677
Anmelder/Applicant/Demandeur//Patentinhaber/Proprietor/Titulaire The Trustees of Columbia University in the City of New York	

COMMUNICATION

The European Patent Office herewith transmits the partial European search report under Rule 46(1) EPC relating to the above-mentioned European patent application.

Copies of the documents cited in the search report are enclosed.

The applicant's attention is drawn to the following:

The search Division informs the applicant that if the European search report is also to cover inventions other than the invention first mentioned in the claims, a further search fee must be paid for each of these inventions, within ONE MONTH after notification of this communication.

If the application has been filed up to 30 June 1999, the search fee in force before 01 July 1999 (EUR 869,-) or the equivalent applicable on the date of payment is payable.

This applies also to the search fees requested under Rule 46(1) EPC.
See also OJ EPO 06/1999, 405.

- ☐ The abstract was modified by the Search Division and the definitive text is attached to the present communication.
- ☐ Additional set(s) of copies of the documents cited in the European search report is (are) enclosed as well.



Note to users of the automatic debiting procedure:

Unless the EPO receives prior instructions to the contrary, the search fee(s) will be debited on the last day of the period for payment. For further details see the Arrangements for the automatic debiting procedure, Supplement to OJ EPO 02/1999.

REGISTERED LETTER

EPO Form 1507.2 (07.99)

Applicants: Takaaki Sato et al.
U.S. Serial No.: 09/230,111
Filed: May 17, 1999
Exhibit 4



The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

1. Claims: 7-13,23,24 (completely) and 1-6,25,26,
77-120 (partially)

Peptide DSENSNFRNEIQSLV, fragments thereof (including ESLV)
and their methods and therapeutical use

2. Claims: 14 (completely) and 1-6,25,26,77-120 (partially)

Peptide IPPDSEDGNEEQSLV, its methods and therapeutical use

3. Claims: 15 (completely) and 1-6,25,26,77-120 (partially)

Peptide DSEMYNFRSQLASVV, its methods and therapeutical use

4. Claims: 16 (completely) and 1-6,25,26,77-120 (partially)

Peptide IDLASEFLFLSNSFL, its methods and therapeutical use

5. Claims: 17 (completely) and 1-6,25,26,77-120 (partially)

Peptide PPTCSQANSGRISTL, its methods and therapeutical use

6. Claims: 18 (completely) and 1-6,25,26,77-120 (partially)

Peptide SDSNMNMNELSEV, its methods and therapeutical use

7. Claims: 19 (completely) and 1-6,25,26,77-120 (partially)

Peptide QNFRTYIVSFV, its methods and therapeutical use

8. Claims: 20 (completely) and 1-6,25,26,77-120 (partially)

Peptide RETIESTV, its methods and therapeutical use

9. Claims: 21 (completely) and 1-6,25,26,77-120 (partially)

Peptide RGFISSLV, its methods and therapeutical use

10. Claims: 22 (completely) and 1-6,25,26,77-120 (partially)

Peptide TIQSVI, its methods and therapeutical use

11. Claims: 27-76 (completely)

Methods of identifying compounds capable of inhibiting
specific binding between a signal-transducing protein and a
cytoplasmic protein containing (G/S/A/E)-L-G-(F/I/L) or
(S/T)-X-(V/I/L)

The problem underlying the present application is to inhibit the



The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:

proliferation of cancer cells. As a solution, compounds that inhibit the interaction between the signal-transduction molecules Fas and FAP-1 are proposed, as these proteins have been identified as important signal-mediators of apoptosis.

Such compounds, however, have already been described in the prior art: In WO 95/34661 a 15-mer peptide of the C-terminus of Fas (amino acids 321-335, i.e. DSENSNFRNEIQSLV) is used to modulate apoptosis.

Therefore, this technical feature can no longer fulfill the requirements of a "special technical feature" in the sense of Article 82 EPC and Rule 30 EPC, linking the different inventions together.

As there are no other features which could fulfill the role of a special technical feature in the sense of Article 82 EPC and Rule 30 EPC, the present application is found to lack unity of invention, giving rise to the subjects as defined.

Since performing a search for all subjects would involve considerable supplementary search effort, a search was performed for the first subject only.



Although claims 89-100 and 109-116 are directed to a method of treatment of the human/animal body (Article 52(4) EPC), the search has been carried out and based on the alleged effects of the compound/composition.

Claim(s) searched completely:
7-13,23,24

Claim(s) searched incompletely:
1-6,25,26,77-120

Claim(s) not searched:
14-22,27-52

Reason for the limitation of the search:

Present claims 1-6,25,26 and 77-120 (partially) relate to compounds and their methods defined by reference to a desirable characteristic or property, namely the ability of inhibiting specific binding between two signal-transducing proteins which contain specific amino acid sequences. Subject-matter of said claims lacks any technical feature in the sense of Article 84 and Rule 29 EPC. An attempt is made to define the compounds by reference to a result to be achieved, i.e. its inhibitory effects of the specific binding between two signal-transducing proteins or by its way of identification. This lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear and belong to the first invention of the application, namely those parts relating to the compounds and methods of claims 7-13,23,24 (completely) and 1-6,25,26,77-120 (partially).



European Patent
Office

**SUPPLEMENTARY
PARTIAL EUROPEAN SEARCH REPORT**
under Rule 46, paragraph 1 of the European Patent
Convention

Application Number

EP 97 93 7999

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
X	WO 95 34661 A (LA JOLLA CANCER RESEARCH FOUNDATION) 21 December 1995 (1995-12-21) * the entire document, particularly page 2, ll. 11-15; page 3, ll. 1-27; page 13, ll. 25-33; page 14, ll. 13-26; page 26, ll. 4-16; page 28, ll. 23-31, examples 1 and 2; figures 6 and 8 *	1-7, 25, 26, 77-120	A61K38/00 A61K39/00 C07K1/00 C07K14/00 C07K17/00 G01N33/53 G01N33/567 G01N33/574
X,D	SATO T ET AL.: "FAP-1: A Protein Tyrosine Phosphatase That Associates with Fas" SCIENCE, vol. 268, 21 April 1995 (1995-04-21), pages 411-415, XP002185190 * the entire document, particularly figure 2A, amino acid sequence (h) *	1-7, 25, 26, 77-120	
P,X	WO 97 11091 A (KIRIN BEER KABUSHIKI KAISHA) 27 March 1997 (1997-03-27) * abstract; figures 2,5-11 *	1-13, 24-26, 77-120	
			TECHNICAL FIELDS SEARCHED (Int.Cl.6)
			C07K A61K G01N
LACK OF UNITY OF INVENTION			
The Search Division considers that the present European patent application does not comply with the requirements of unity of invention and relates to several inventions or groups of inventions, namely:			
see sheet B			
The present partial European search report has been drawn up for those parts of the European patent application which relate to the invention first mentioned in the claims.			
Place of search THE HAGUE		Date of completion of the search 14 December 2001	Examiner Schmidt, H
CATEGORY OF CITED DOCUMENTS			
X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document			
T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons ----- & : member of the same patent family, corresponding document			

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 97 93 7999

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.
The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

14-12-2001

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9534661 A	21-12-1995	US 5747245 A	05-05-1998
		US 5632994 A	27-05-1997
		AU 2705395 A	05-01-1996
		CA 2192844 A1	21-12-1995
		DE 769060 T1	24-09-1998
		EP 0769060 A1	23-04-1997
		JP 10504446 T	06-05-1998
		WO 9534661 A1	21-12-1995
		US 5876939 A	02-03-1999
WO 9711091 A	27-03-1997	JP 11171896 A	29-06-1999
		AU 7000896 A	09-04-1997
		WO 9711091 A1	27-03-1997